

## REMARKS

Claims 1 thru 9 are currently pending in the application. Claims 1 and 9 have been amended. The forgoing amendments are made to more clearly state the subject matter being claimed. The specific grounds for rejection and Applicant's response to them are set forth in detail below.

1. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states that, "The recitation of hyaluronic acid having molecular weight of greater than or equal to 750,000 Daltons is new matter. Although applicants in the amendment that inserted the molecular indicated that there is support for the amendment in the specification as originally filed, the specific page and lines in the specification providing the support was not stated and Examiner does not find support for the amendment.".

Applicant respectfully disagrees. The recitation of the phrase "hyaluronic acid having a molecular weight of greater than or equal to 750,000 Daltons" in the claims is not new matter. Literal support can be found in the specification of the application at page 17, line 37 (890 kD); page 29, line 28 (890 kD); page 39, line 31 (750 kD); and page 40, line 16 (750 kD). Reconsideration is respectfully requested.

2. Claims 1, 6, 7 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Turley et al. (US 6,475,795 B 1).

The Examiner states that, "Turley discloses pharmaceutical composition that comprises anti-sense nucleic acid bound to hyaluronic acid for treating diseases or conditions treatable using

gene therapy (column 6, line 60 to column 7 line 10; column 2, line 62 to column 3 line 7 and claims 1-8). Turley specifically discloses that hyaluronan having a molecular weight of between 150,000 Daltons and 750,000 Daltons is preferred (column 7, lines 11-15 and 33; column 9, lines 37-40; claims 2 and 3). In column 7, line 64, hyaluronan having molecular weight of between 500,000 and 800,000 is used and larger molecular weight hyaluronan can be used in Turley except for hyaluronan having molecular weight exceeding 1,000,000 because at greater than 1,000,000, the hyaluronan self aggregates (column 10, lines 7-14). On the basis that Turley disclose larger molecular weight hyaluronan up to 1,000,000 but not exceeding, 1,000,000, there is then a disclosure for use of hyaluronan having molecular weight of greater than 750,000 in the formulation of Turley. Therefore, Turley meets the limitations of the designated claims. The previous rejection will remain when the new matter is removed.".

Applicant has amended independent claims 1 and 9 to include a limitation which qualifies the cytotoxic or neoplastic agents as "non-polynucleic acid based". As such, the claims of the present application, as amended, do not encompass polynucleotides (which includes anti-sense molecules) and, consequently, the Turley reference does not anticipate amended independent claims 1 and 9, as well as dependent claims 6 and 7..

3. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falk et al. (US 5,985,850).

The Examiner states that, "Falk discloses injectable formulations comprising anti-cancer agent or chemotherapeutic agent and hyaluronic acid (column 10, lines 8-59). The preferred molecular weight for the hyaluronan is less than 750,000 Daltons (claims 142, 83, 84 and 92). There is no demonstration in applicant's specification that a molecular weight of greater than or equal to 750,000 Dalton provides unusual and unexpected results. A molecular weight of greater than or equal to 750,000 Daltons is not inventive over the disclosure in the prior art of a molecular weight of less than 750,000. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a composition comprising hyaluronic acid and anti-cancer agent to a subject in need thereof. One having ordinary skill in the art would have been motivated to use hyaluronic acid having the appropriate molecular weight that would provide the desired therapeutic effect and viscosity of the composition.".

In Examples 2, 3 and 6 of the Applicant's specification, cytotoxic or anti-neoplastic agents were prepared and used in combination with Hyaluronic Acid with molecular weights of 890 kD, 890 kD and 750kD, respectively. In addition, Applicant is concurrently submitting with this Amendment a Declaration under 37 C.F.R. §1.32 which describes the use and unexpected efficacy of cytotoxic or anti-neoplastic agents when administered to cancer cells with high molecular weight Hyaluronic Acid (824 kD) as opposed to administration with low molecular weight Hyaluronic Acid (30 kD). Given the lack of reference in the prior art to the co-administration of higher molecular weight Hyaluronic Acid with cytoplastic or anti-neoplastic agents, Applicant respectfully disagrees with the Examiner's position and requests reconsideration.

4. Claims 1-9 are rejected under in the alternative, under 35 U.S.C. 103(a) as obvious over Turley et al. (US 6,475,795 B1).

The Examiner states that, "Turley is described above. There is a disclosure for composition comprising hyaluronic acid having molecular weight of 500,000 to 800,000 Daltons and a composition that may have hyaluronan having preferred molecular weight of between 15,000 and 750,000 Daltons. Since molecular weight of between 150,000 and 750,000 Daltons is less than 750,000 Daltons, Turley renders the claims obvious because a molecular weight of greater than 750,000 Daltons is not inventive over the prior art. There is no demonstration in applicant's specification that a molecular weight of greater than or equal to 750,000 Dalton provides unusual and unexpected results. A molecular weight of greater than or equal to 750,000 Daltons is not inventive over the disclosure in the prior art of a molecular weight of between 150,000 and 750,000 Daltons. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a composition comprising hyaluronic acid and anti-sense agent to a subject in need thereof. One having ordinary skill in the art would have been motivated to use hyaluronic acid having the appropriate molecular weight that would provide the desired therapeutic effect and viscosity of the composition and where the molecular weight does not exceed 1,000,000 in order to avoid aggregation of the hyaluronan.".

Applicant has amended independent claims 1 and 9 to include a limitation which qualifies the cytotoxic or neoplastic agents as "non-polynucleic acid based". As such, the Turley reference cannot be used a basis in forming a rejection based on obviousness. The amended claims have obviated the 103 rejection of claims 1-9. Furthermore, Applicant has concurrently submitted a Declaration under 37 C.F.R. §1.32, as mentioned above. This Declaration presents evidence that unexpected efficacy of cytotoxic or anti-neoplastic agents can be achieved when administered to cancer cells with high molecular weight Hyaluronic Acid (824 kD) as opposed to administration with low molecular weight Hyaluronic Acid (30 kD). Applicant respectfully requests reconsideration.

Applicants request the entry of the changes to the claims requested above. No new matter has been added by the amendments to the claims.

If for any reason an additional fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

  
\_\_\_\_\_  
Gregory B. Butler, PhD (Reg. 34,558)  
EDWARDS & ANGELL, LLP  
P.O. Box 9169  
Boston, MA 02209  
(617) 439-4444

Date: October 28, 2005

508774v1